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ATTORNEY'S DOCKET NUMBER

454313-3156

**TRANSMITTAL LETTER TO THE UNITED STATES  
DESIGNATED/ELECTED OFFICE (DO/EO/US)  
CONCERNING A FILING UNDER 35 U.S.C. 371**

INTERNATIONAL APPLICATION NO.

PCT/FR98/02868

INTERNATIONAL FILING DATE

23 DECEMBER 1998

U.S. APPLICATION NO. (If known see 37 C.F.R. 1.5)

09/582130

(EARLIEST) PRIORITY DATE CLAIMED

24 DECEMBER 1997

TITLE OF INVENTION

**USE OF POLYPHENOL COMPOUNDS OR DERIVATIVES THEREOF AS  
FREE-RADICAL SCAVENGERS IN CIGARETTE FILTERS**

APPLICANTS FOR DO/EO/US

**Imam EMAMI**

Applicants herewith submit to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
  2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
  3. ☒ This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
  4. ☒ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
  5. ☒ A copy of the International Application as filed (35 U.S.C. 371(c)(2))
    - a. ☒ is transmitted herewith (required only if not transmitted by the International Bureau).
    - b. ☐ has been transmitted by the International Bureau.
    - c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
  6. ☒ A translation of the International Application into English (35 U.S.C. 371(c)(2)), including 1 sheet of formal drawing and a copy of the International Search Report.
  7. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
    - a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
    - b. ☐ have been transmitted by the International Bureau.
    - c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
    - d. ☒ have not been made and will not be made.
  8. ☐ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
  9. ☐ An oath or declaration of the inventors (35 U.S.C. 371(c)(4)).
  10. ☐ The annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).
- Items 11. to 16. below concern other document(s) or information included:**
11. ☒ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
  12. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
  13. ☒ A FIRST preliminary amendment.  
☐ A SECOND or SUBSEQUENT preliminary amendment.
  14. ☐ A substitute specification.
  15. ☐ A change of power of attorney and/or address letter.
  16. ☒ Other items or information:  
PCT/ISA/210, PCT/IB/304, PCT/IPEA/409  
References for IDS, copy of French Search Report

**EXPRESS MAIL**

Mailing Label Number: EL560704748US

Date of Deposit: June 22, 2000

I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" Service under 37 CFR 1.10 on the date indicated above and is addressed to the Assistant Commissioner for Patents and Trademarks, Box PCT Washington, DC 20231.

*Charles Jackson*  
(Typed or printed name of person mailing paper or fee)

*Charles Jackson*  
(Signature of person mailing paper or fee)

U.S. APPLICATION NO. (If known, see 37 C.F.R. 1.50)

INTERNATIONAL APPLICATION NO.  
PCT/FR98/02868ATTORNEY'S DOCKET NO.  
454313-3156

09/582130

17. ☒ The following fees are submitted:

(CALCULATIONS /PTO USE ONLY)

Basic National Fee (37 CFR 1.492(a)(1)-(5):

Search Report has been prepared by the EPO or JPO.....\$840.00 (\$840.00

International preliminary examination fee paid to USPTO (37 CFR 1.482) (\$700.00

No international preliminary examination fee paid to USPTO (37 CFR 1.482) (

but international search fee paid to USPTO (37 CFR 1.445(a)(2))...\$770.00 (

Neither international preliminary examination fee (37 CFR 1.482) nor (

international search fee (37 CFR 1.445(a)(2)) paid to USPTO.....\$1040.00 (

International preliminary examination fee paid to USPTO (37 CFR 1.482) (

and all claims satisfied provisions of PCT Article 33(2)-(4).....\$96.00 (

ENTER APPROPRIATE BASIC FEE AMOUNT = (\$ 840.00

Surcharge of \$130.00 for furnishing the oath or declaration later than ☐ 20 ☐ 30 (\$ /  
months from the earliest claimed priority date (37 CFR 1.492(e)).

12 Claims /Number Filed / Number Extra /Rate (

Total Claims / 17 - 20 = / 0 /X \$18.00 (\$ 0.00

Independent Claims / 2- 3 = / 0 /X \$78.00 (\$ 0.00

Multiple dependent claim(s) (if applicable) /+ \$260.00 (\$

TOTAL OF ABOVE CALCULATIONS = (\$840.00

Reduction by 1/2 for filing by small entity, if applicable. Verified Small Entity ( \$420.00/  
statement must also be filed. (Note 37 CFR 1.9, 1.27, 1.28). ( /

SUBTOTAL = (\$420.00

Processing fee of \$130.00 for furnishing the English translation later than ( /  
☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492(f)).+ (\$ /

TOTAL NATIONAL FEE = (\$420.00

Fee for recording the enclosed assignments (37 CFR 1.21(h)). The assignment (\$ 0.00/  
must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 per property + (\$ /

TOTAL FEES ENCLOSED = (\$420.00

(Amount to be: /

(refunded /\$

(charged /\$

a. ☒ Our check in the amount of \$420.00 to cover the above fees is enclosed.b. ☐ Please charge my Deposit Account No. 50-0320 in the amount of \$ to cover the above fees.

A duplicate copy of this sheet is enclosed.

c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any  
overpayment to Deposit Account No. 50-0320. A duplicate copy of this sheet is enclosed.NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and  
granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

WILLIAM S. FROMMER  
FROMMER LAWRENCE & HAUG LLP  
745 FIFTH AVENUE  
NEW YORK, NEW YORK 10151

SIGNATURE

WILLIAM S. FROMMER  
NAME

Dated: June 21, 2000

25.506  
REGISTRATION NUMBER

Form PTO-1390 (REV 10-96)

**VERIFIED STATEMENT CLAIMING SMALL ENTITY STATUS**  
**(37 CFR 1.9(f) & 1.27(c))--SMALL BUSINESS CONCERN**

Docket Number (Optional)

Applicant or Patentee: BIOSYNTHETICSerial or Patent No.: 582130Filed or Issued: June 22, 2000Title: "Use of polyphenol compounds or derivatives thereof as free-radical scavengers in cigarette filters"

I hereby declare that I am

- ☒ the owner of the small business concern identified below:  
☐ an official of the small business concern empowered to act on behalf of the concern identified below:

NAME OF SMALL BUSINESS CONCERN BIOSYNTHETICADDRESS OF SMALL BUSINESS CONCERN 41 rue Barrault 75013 PARIS France

I hereby declare that the above identified small business concern qualifies as a small business concern as defined in 13 CFR 121.12, and reproduced in 37 CFR 1.9(d), for purposes of paying reduced fees to the United States Patent and Trademark Office, in that the number of employees of the concern, including those of its affiliates, does not exceed 500 persons. For purposes of this statement, (1) the number of employees of the business concern is the average over the previous fiscal year of the concern of the persons employed on a full-time, part-time or temporary basis during each of the pay periods of the fiscal year, and (2) concerns are affiliates of each other when either, directly or indirectly, one concern controls or has the power to control the other, or a third party or parties controls or has the power to control both.

I hereby declare that rights under contract or law have been conveyed to and remain with the small business concern identified above with regard to the invention described in:

- ☐ the specification filed herewith with title as listed above.  
☒ the application identified above.  
☐ the patent identified above.

If the rights held by the above identified small business concern are not exclusive, each individual, concern or organization having rights in the invention must file separate verified statements averring to their status as small entities, and no rights to the invention are held by any person, other than the inventor, who would not qualify as an independent inventor under 37 CFR 1.9(c) if that person made the invention, or by any concern which would not qualify as a small business concern under 37 CFR 1.9(d), or a nonprofit organization under 37 CFR 1.9(e).

Each person, concern or organization having any rights in the invention is listed below:

- ☒ no such person, concern, or organization exists.  
☐ each such person, concern or organization is listed below.

Separate verified statements are required from each named person, concern or organization having rights to the invention averring to their status as small entities. (37 CFR 1.27)

I acknowledge the duty to file, in this application or patent, notification of any change in status resulting in loss of entitlement to small entity status prior to paying, or at the time of paying, the earliest of the issue fee or any maintenance fee due after the date on which status as a small entity is no longer appropriate. (37 CFR 1.28(b))

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

BIOSYNTHETIC

41 rue Barrault 75013 PARIS France

NAME OF PERSON SIGNING IMAMI Imam

General Director

TITLE OF PERSON IF OTHER THAN OWNER

ADDRESS OF PERSON SIGNING

SIGNATURE

DATE 08/08/2000

9716532

Form A

**VERIFIED STATEMENT CLAIMING SMALL ENTITY STATUS  
(37 CFR 1.9(f) & 1.27(b))--INDEPENDENT INVENTOR**

Docket Number (Optional)

Applicant or Patentee: EMAMI Imam

Serial or Patent No.: 582130

Filed or Issued: June 22, 2000

Title: "Use of polyphenol compounds or derivatives thereof as free-radical scavengers in cigarette filters".

As a below named inventor, I hereby declare that I qualify as an independent inventor as defined in 37 CFR 1.9(c) for purposes of paying reduced fees to the Patent and Trademark Office described in:

- ☐ the specification filed herewith with title as listed above.  
☒ the application identified above.  
☐ the patent identified above.

I have not assigned, granted, conveyed or licensed and am under no obligation under contract or law to assign, grant, convey or license, any rights in the invention to any person who would not qualify as an independent inventor under 37 CFR 1.9(c) if that person had made the invention, or to any concern which would not qualify as a small business concern under 37 CFR 1.9(d) or a nonprofit organization under 37 CFR 1.9(e).

Each person, concern or organization to which I have assigned, granted, conveyed, or licensed or am under an obligation under contract or law to assign, grant, convey, or license any rights in the invention is listed below:

- ☒ No such person, concern, or organization exists.  
☐ Each such person, concern or organization is listed below.

Separate verified statements are required from each named person, concern or organization having rights to the invention averring to their status as small entities. (37 CFR 1.27)

I acknowledge the duty to file, in this application or patent, notification of any change in status resulting in loss of entitlement to small entity status prior to paying, or at the time of paying, the earliest of the issue fee or any maintenance fee due after the date on which status as a small entity is no longer appropriate. (37 CFR 1.28(b))

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

(EMAMI Imam)

NAME OF INVENTOR

Signature of inventor

Date

August 11, 2000

NAME OF INVENTOR

Signature of inventor

Date

NAME OF INVENTOR

Signature of inventor

Date

09/582130

526 Rec'd PCT/PTO 22 JUN 2000

Attorney Docket No. 454513-3156

New Patent Application filed **June 22, 2000**, entitled:

**USE OF POLYPHENOL COMPOUNDS OR DERIVATIVES  
THEREOF AS FREE-RADICAL SCAVENGERS IN CIGARETTE FILTERS**

corresponding to PCT Application No. PCT/FR98/02868

filed December 23, 1998

Express Mail No.: EL560704748US

Date of Deposit: June 22, 2000

I hereby certify that this application and the accompanying papers are being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to:

Box PCT  
Assistant Commissioner for Patents  
Washington, D.C. 20231.

Charles Jackson

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant(s) : Imam EMAMI  
Int'l Appln. No. : PCT/FR98/02868  
Int'l Filing Date : 23 December 1998  
Title of Invention : USE OF POLYPHENOL COMPOUNDS OR  
DERIVATIVES THEREOF AS FREE-RADICAL  
SCAVENGERS IN CIGARETTE FILTERS

745 Fifth Avenue  
New York, NY 10151  
September 30, 1999

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Date of Deposit: June 22, 2000

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Charles Jackson  
(Typed or printed name of person mailing paper or fee)

Charles Jackson  
(Signature of person mailing paper or fee)

**PRELIMINARY AMENDMENT**

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

Before the issuance of the first Official Action, please amend the above-identified application as follows:

**IN THE CLAIMS:**

Claim 6, line 1, please delete "either of Claims 2 and 3" and insert --Claim 2--;

Claim 8, line 1, please delete "one of Claims 1, 6 and 7" and insert --Claim 1--;

Claim 9, line 1, please delete "any one of the preceding claims" and insert --Claim

1--;

Claim 10, line 1, please delete "any one of the preceding claims" and insert --

Claim 1--;

Claim 11, lines 2-3, please delete "any one of the preceding claims" and insert --

Claim 1--;

Please add the following new claims:

--13. Use according to Claim 6, in which the said plant extract is obtained by extraction in an alcoholic or aqueous-alcoholic solvent.

14. Use according to Claim 2, in which the polyphenol compounds are coupled to a carrier of polymer type.

15. Use according to Claim 2, in which the polyphenol compounds or derivatives thereof are incorporated into a cigarette filter in a proportion of from 0.5mg to 0.1 gram, preferably 0.01 gram.

16. Process for preparing a cigarette filter, in which polyphenol compounds as defined in Claim 2 are incorporated into the said cigarette filter.

17. Cigarette filter obtained by the process of Claim 16.--


**REMARKS**

This application includes multiple claim dependencies. The amendment removes the multiple claim dependencies, and the filing fee for this application was computed on the basis that no dependent claim depends from more than one preceding claim.

Entry of this Amendment and an early examination on the merits are respectfully solicited. Please charge any additional fees required for this amendment or credit any overpayment to Deposit Account No. 50-0320.

Respectfully submitted,

FROMMER LAWRENCE & HAUG LLP  
Attorneys for Applicant

By:   
William S. Frommer  
Reg. No. 25,506  
Tel. (212) 588-0800

Use of polyphenol compounds or derivatives thereof  
as free-radical scavengers in cigarette filters

The present invention relates to the use of  
5 polyphenol compounds or derivatives thereof as free-  
radical scavengers in cigarette filters.

Many polyphenol compounds are known for their  
beneficial properties in fields as varied as hyperten-  
sion, hypercholesterolaemia, involved in cardiovascular  
10 diseases, viral infections or inflammatory phenomena.  
The anti-lipoperoxidative and anti-carcinogenic activi-  
ties of certain polyphenols have also been described.

Moreover, the incorporation of polyphenols from  
green tea into a cigarette filter has been envisaged to  
15 eliminate the unpleasant odour of cigarettes.

The authors of the present invention have now  
discovered that the incorporation of polyphenols or  
derivatives thereof in a cigarette filter makes it  
possible efficiently to remove the free radicals of the  
20 cytotoxic molecules of cigarette smoke during their  
passage through the filter.

The subject of the present invention is thus  
the use of polyphenol compounds as free-radical  
scavengers in cigarette filters.

25 The polyphenols used in accordance with the  
present invention can preferably be chosen from  
carnosol, rosmanol, rosmarinic acid and carnosic acid,  
and derivatives thereof.

The term "derivatives" in particular means  
30 compounds derived from polyphenol compounds by sub-  
stituting the hydrogen atom of at least one of the  
hydroxyl groups of the polyphenol compounds with a C<sub>1</sub>-C<sub>6</sub>  
alkyl group or a (C<sub>1</sub>-C<sub>4</sub> alkyl)carbonyl group. Acetates  
such as carnosic acid acetates and rosmarinic acid  
35 acetates are preferred derivatives of the polyphenol  
compounds used in accordance with the invention.

The term "derivatives" of the polyphenols used  
in accordance with the invention such as carnosol,



rosmanol, rosmarinic acid and carnosic acid also means the isomers of the said polyphenols such as, in particular, epirosmanol and isorosmanol (Nakatani et al., Agric. Biol. Chem., 1984, vol. 48, No. 8, pp. 2081-2085).

These compounds can be obtained by conventional chemical synthesis or by biotechnological synthesis, according to processes that are known to those skilled in the art. They can also be isolated from plant extracts.

The said polyphenols can also be used according to the present invention in the form of a plant extract, preferably an extract of a plant from the Labiatae family, in particular such as an extract of rosemary (*Rosmarinus officinalis* L.).

Such a plant extract can be obtained by extraction with a polar solvent such as an alcoholic or aqueous-alcoholic solvent. The alcohol used as solvent can in particular be ethanol. This extract can also advantageously be obtained using supercritical carbon dioxide and, in that case, is richer in polyphenol compounds.

The plant extract used according to the invention can preferably be obtained by extraction with a polar solvent followed by an extraction with supercritical CO<sub>2</sub>.

The extraction of rosemary is preferably carried out on dried plants, for example on rosemary branches, chopped and dried in the sun for 4 to 5 days.

The polyphenol compounds or derivatives thereof, obtained by chemical or biotechnological synthesis or by extraction from plants, can be used alone or as a mixture in accordance with the invention.

Preferably, a mixture of carnosol, carnosic acid and rosmarinic acid may be used advantageously.

The polyphenol compounds or derivatives thereof can be used in free form or can be conjugated or coupled to a carrier, making it possible to increase the weight of the polyphenol-carrier assembly.

Microbeads may in particular serve as carrier. They may be made, for example, of plastic (polystyrene or the like) or of glass.

5 The polyphenol compounds can be incorporated into the cigarette filters in a proportion of from 0.5 mg to 0.5 gram, preferably 0.002 gram to 0.1 gram, preferably 0.01 gram.

10 When the polyphenol compounds are dissolved in a solvent, the cigarette filter can advantageously be soaked with the said solvent containing the polyphenols, followed by evaporation of the said solvent. More particularly, the cigarette filter can be soaked with an alcoholic or aqueous-alcoholic plant extract and then subjected to evaporation of the alcoholic or  
15 aqueous-alcoholic solvent.

The polyphenol compounds or derivatives thereof can also be dissolved in a saturated oil, and thus incorporated into the cigarette filter.

20 A subject of the invention is also a process for preparing a cigarette filter, in which polyphenol compounds chosen from carnosol, rosmanol, rosmarinic acid and carnosic acid, and derivatives thereof, are incorporated into the said cigarette filter.

25 Another subject of the invention is a cigarette filter obtained by the above process. Such a filter makes it possible to reduce the amount of free-radical molecules present in cigarette smoke.

30 The authors of the present invention have discovered that polyphenols or derivatives thereof incorporated into a cigarette filter trap the free radicals of the cytotoxic molecules present in cigarette smoke, both in the aqueous phase and in the solid phase of the smoke, which consists essentially of tars.

35 These cytotoxic molecules promote the development of cancers in smokers, in particular lung cancer.

The polyphenols or derivatives thereof incorporated into a cigarette filter also exhibit, firstly, inhibition of the activity of the carcinogenic

compounds by reducing the formation of heterocyclic amines during the combustion of the tobacco, and, secondly, a detoxification of the carcinogenic compounds, such as benzopyrene.

5           The figure and the examples which follow illustrate the invention without limiting its scope.

          The attached figure is a graph representing the intensity of the signal, in electron paramagnetic resonance, of the tert-butyloxy radicals in the gas  
10       phase of the cigarette smoke as a function of the amount of extract of rosemary incorporated into the filter.

#### EXAMPLE

15

##### **A - Preparation of an extract of rosemary**

          Spikes of rosemary (*Rosmarinus officinalis* L.) are subjected to extraction with ethanol at 65°C. The volume of ethanol used (in litres) corresponds to five  
20       times the weight in kg of the rosemary spikes.

          The extract is then purified and enriched in polyphenols by selective extraction with supercritical CO<sub>2</sub>. Depending on the temperature adjustment made between 40°C and 100°C and on the pressure adjustment  
25       made between 1 and 170 bar, the extract is purified and selectively enriched in its various components.

          Such an extract contains the following compounds:

- 30           - carnosol,
- rosmanol,
- rosmadial,
- carnosic acid,
- genkwanine,
- rosmarinic acid, etc.

35           The proportions of these various components vary according to the rosemary plant used. Generally, an extract comprising about 25% rosmarinic acid, about 10% carnosic acid and about 5% carnosol is obtained.

B - Incorporation of the extract into a cigarette filter

A cigarette filter is soaked either with the extract prepared, the ethanol then being evaporated off, or with an oily phase based on Crodamol® (Française d'Arômes et Parfums), in which a powder obtained by drying the extract prepared above is dissolved.

C - Efficacy of the filter containing the polyphenols

1. Computer-assisted modelling:

The efficacy of the cigarette filter thus prepared is demonstrated in a first stage by computer-assisted modelling, according to the Monte-Carlo method, which makes it possible to calculate the number of encounters between a carcinogenic target molecule and a polyphenol compound used in accordance with the invention.

The number of cytotoxic molecules containing free radicals present in the cigarette smoke was calculated on either side of the filter.

The number of cytotoxic molecules is a function of the volume of smoke passing through the filter, the volume of the filter, the concentration of cytotoxic molecules in the smoke and the concentration of polyphenols in the filter.

The authors of the present invention have thus shown that 0.01 g of the extract of rosemary incorporated into a cigarette filter makes it possible to reduce the level of molecules containing cytotoxic free radicals in the cigarette smoke by more than 70%.

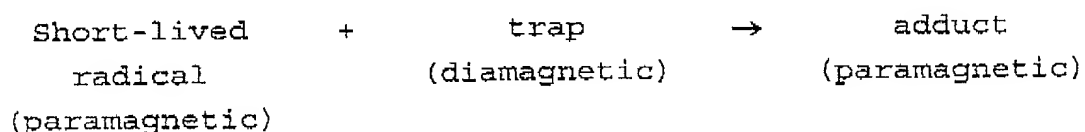
2. Electron paramagnetic resonance:

The radical-scavenging activity of the extract comprising carnosol, rosmarinic acid and carnosic acid was confirmed by Electron Paramagnetic Resonance (EPR) spectroscopy, optionally using the "spin-trapping"

method.

*a. Materials and methods*

EPR is a technique which makes it possible to study paramagnetic substances directly or indirectly. Paramagnetic compounds are molecules containing a single unpaired electron in their outer valence shell. Such substances are denoted by the term "radicals". When these radicals have very short lifetimes (very much less than one second), it is advantageous to use the "spin-trapping" technique. This consists in using traps capable of stabilizing the radicals produced by the formation of an adduct, and thus of measuring them over several minutes. This reaction takes place in the following way:



DMPO (5,5'-dimethylpyrroline N-oxide) was used as the "trap".

*Radical-scavenging activity on the radicals produced in the gas phase of cigarette smoke:*

The device for trapping the radicals of the gas phase of cigarette smoke is described in Pryor et al., Environmental Health Perspectives, 1976, vol. 16, pp. 161-175.

A cigarette is placed at the end of such a device, and the gas phase of the smoke, after passing through a Cambridge filter (finer than a cigarette filter in order to retain the tars), is dissolved in a "spin-trap" benzene solution.

For each measurement the DMPO is adjusted to a concentration of 32 mM in a solution of benzene and the gas phase of two cigarettes is used.

**Radical-scavenging activity on the semiquinone radical contained in the solid phase of the cigarette filter:**

Besides the free radicals produced in the gas phase of the smoke, free radicals are also present in the tars which are partially stopped by the solid phase of conventional commercial filters.

The radical, which is mainly present in these tars and which is responsible for a carcinogenic activity that has been well-established to date, is of semiquinone nature. This semiquinone, which has a long lifetime, is able to react in cells and thus produce harmful species such as oxygen-containing radicals.

A second series of experiments consisted in studying the semiquinone radical contained in the solid phase of the filter. This study does not require the use of traps. Specifically, the detection of the radical, which has a very long lifetime, is made *in situ* on the filter recovered.

**b. Results**

***Efficacy in solution of the extract of rosemary in trapping free radicals produced in the gas phase***

In order to evaluate the ability of the extract of rosemary to trap the radicals in the gas phase of cigarette smoke in solution in benzene, the intensity of the EPR signal of the tert-butyloxy radicals was evaluated as a function of the amount of extract of rosemary added to the trapping solution, expressed in grams of dried powdered extract.

A decrease in the signal indicates that the extract of rosemary has a higher radical-trapping rate than that of DMPO (cf. figure).

***Efficacy of the extract of rosemary in trapping radicals produced in the gas phase, after impregnating the filter with dried extract of rosemary dissolved in Crodamol®:***

The filter was impregnated with 250 µl of the Crodamol®-based lipid phase, containing 10 mg/ml of

dried powdered extract of rosemary.

EPR analysis of the spectrum of the tert-butyloxy ( $t\text{BuO}^\circ$ ) radical dissolved in benzene made it possible to observe a 65% decrease in the signal of the  
5 DMPO/ $t\text{BuO}^\circ$  adduct. This result shows that the extract of rosemary used is effective in inhibiting the formation of the  $t\text{BuO}^\circ$  radicals.

*Efficacy of the extract of rosemary in trapping radicals produced in the solid phase, after  
10 impregnating the filter with dried extract of rosemary dissolved in Crodamol®:*

In parallel with the experiment carried out above, the signal of the semiquinone radical present in the cigarette filter was evaluated.

15 A decrease of about 63% in the semiquinone signal was observed after treatment of the filter with the extract of rosemary. Furthermore, it is interesting to note that no new signals appear which could indicate the formation of new radicals due to the trapping by  
20 the extract of rosemary. Consequently, these results show that the extract of rosemary is active as regards its ability to quench the semiquinone signal, and that it does not undergo, during this reaction, any conversion generating a new radical.

CLAIMS

1. Use of polyphenol compounds or derivatives thereof present in the form of an extract of rosemary, as free-radical scavengers in cigarette filters.
- 5 2. Use of polyphenol compounds chosen from carnosol, rosmanol, rosmarinic acid and carnosic acid, and derivatives thereof, as free-radical scavengers in cigarette filters.
- 10 3. Use according to Claim 2, in which the polyphenol compounds consist of a mixture of carnosol, carnosic acid and rosmarinic acid.
4. Use according to Claim 2, in which the free-radical scavengers are in the form of a mixture composed totally or partly of carnosol.
- 15 5. Use according to Claim 2, in which the free-radical scavengers are in the form of a mixture composed totally or partly of carnosic acid.
6. Use according to either of Claims 2 and 3, in which the polyphenol compounds are present in the form of a plant extract.
- 20 7. Use according to Claim 4, in which the said plant extract is an extract of rosemary.
8. Use according to one of Claims 1, 6 and 7, in which the said plant extract is obtained by extraction in an alcoholic or aqueous-alcoholic solvent.
- 25 9. Use according to any one of the preceding claims, in which the polyphenol compounds are coupled to a carrier of polymer type.
10. Use according to any one of the preceding claims, in which the polyphenol compounds or derivatives thereof are incorporated into a cigarette filter in a proportion of from 0.5 mg to 0.1 gram, preferably 0.01 gram.
- 30 11. Process for preparing a cigarette filter, in which polyphenol compounds as defined in any one of the preceding claims are incorporated into the said cigarette filter.
- 35



ART 34 AMDT

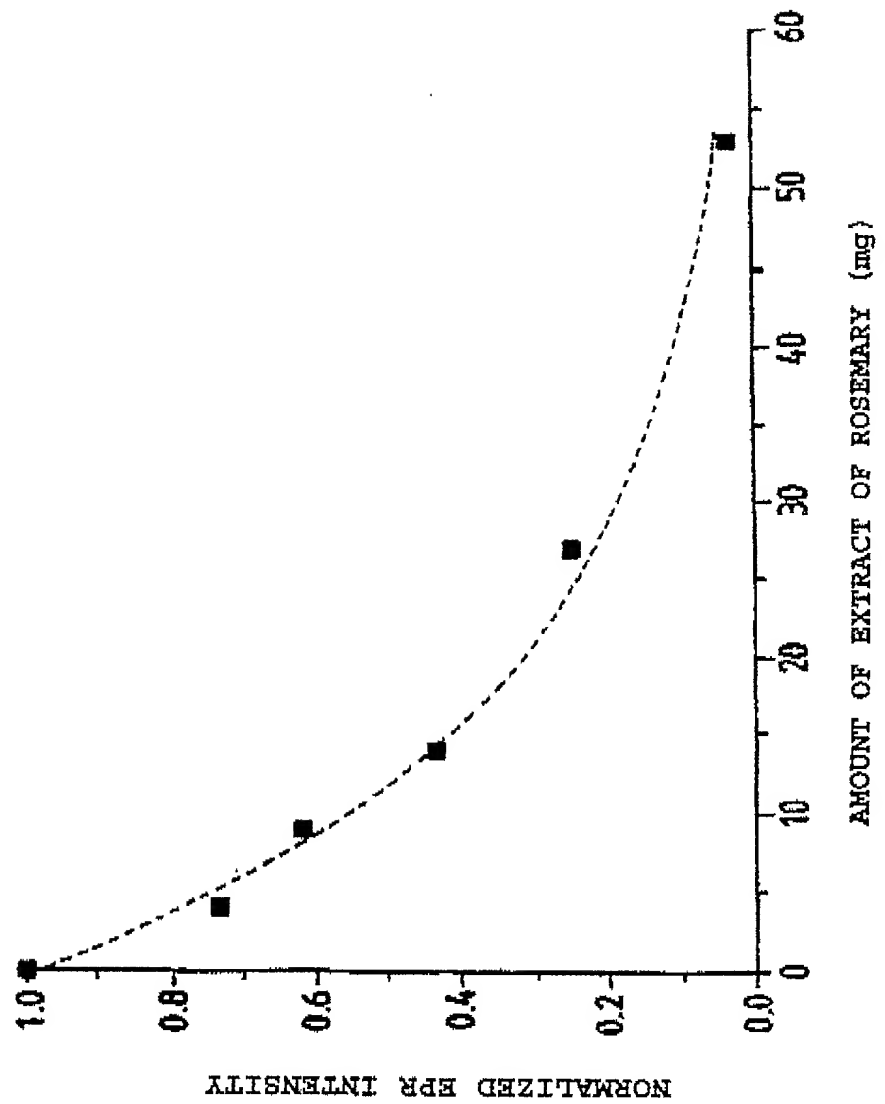
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12. Cigarette filter obtained by the process according to Claim 11.

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AMENDED SHEET

TOTAL 1



Imami: 8/25/2000 22 3528

**DECLARATION FOR PATENT APPLICATION (JOINT OR SOLE)**  
(Under 37 CFR § 1.63; with Power of Attorney)  
**FROMMER, LAWRENCE & HAUG LLP. File No. 454313-2060**

As a below named inventor, I hereby declare that:  
My residence, post office address and citizenship are as stated below next to my name,  
I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention ENTITLED: "Use of polyphenol compounds or derivatives thereof as free-radical scavengers in cigarette filters".

the specification of which

\_\_\_\_\_ is attached hereto.

X \_\_\_\_\_ was filed on 22/06/2000

582130

as International Application Serial No. \_\_\_\_\_

with amendment(s) through \_\_\_\_\_ (if applicable, give dates).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose to the United States Patent and Trademark Office all information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, Sec. 1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, § 119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

Prior Foreign Application(s) [list additional applications on separate page]: Priority Claimed:  
Number: Country: Filed (Day/Month/Year): Yes No

97 16 522 FRANCE

24 December 1997

Yes

I hereby claim the benefit under Title 35, United States Code, § 120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code § 112, I acknowledge the duty to disclose to the United States Patent and Trademark Office all information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, Sec. 1.56, which became available between the filing date of the prior application and the national or PCT international filing date of this application:

Prior U.S. Application(s) [list additional applications on separate page]:  
Appln. Ser. No.: Filed (Day/Month/Year): Status:(patented, pending, abandoned):

PCT/FR98/02868

23 December 1998

Pending

I hereby appoint William S. Frommer, Registration No. 25,506, and FROMMER, LAWRENCE & HAUG LLP, or their duly appointed associate, my attorneys, with full power of substitution and revocation, to prosecute this application, to make alterations and amendments therein, to file continuation and divisional applications thereof, to receive the Patent, and to transact all business in the Patent and Trademark Office and in the Courts in connection therewith, and specify that all communications about the application are to be directed to the following correspondence address:

William S. Frommer, Esq.  
c/o FROMMER, LAWRENCE & HAUG LLP  
745 Fifth Avenue  
New York, New York 10151

Direct all telephone calls  
to: (212)588-0800 to the  
attention of:

William S. Frommer

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

INVENTOR(S):

Signature: [Signature] Date: 08/08/2000  
Full name of sole or first inventor: EMAMI Imam  
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Citizenship: French

Signature: \_\_\_\_\_ Date: \_\_\_\_\_  
Full name of 2nd joint inventor (if any): \_\_\_\_\_  
Residence: \_\_\_\_\_  
Citizenship: \_\_\_\_\_

[Similarly list additional inventors on separate page]  
Post Office Address(es) of inventor(s):  
[if different from residence] Same

Note: In order to qualify for reduced fees available to Small Entities, each inventor and any other individual or entity having rights to the invention must also sign an appropriate separate "Verified Statement (Declaration) Claiming [or Supporting a Claim by Another for] Small Entity Status" form [e.g. for Independent Inventor, Small Business Concern, Nonprofit Organization, individual Non-Inventor].